

Figure 1A

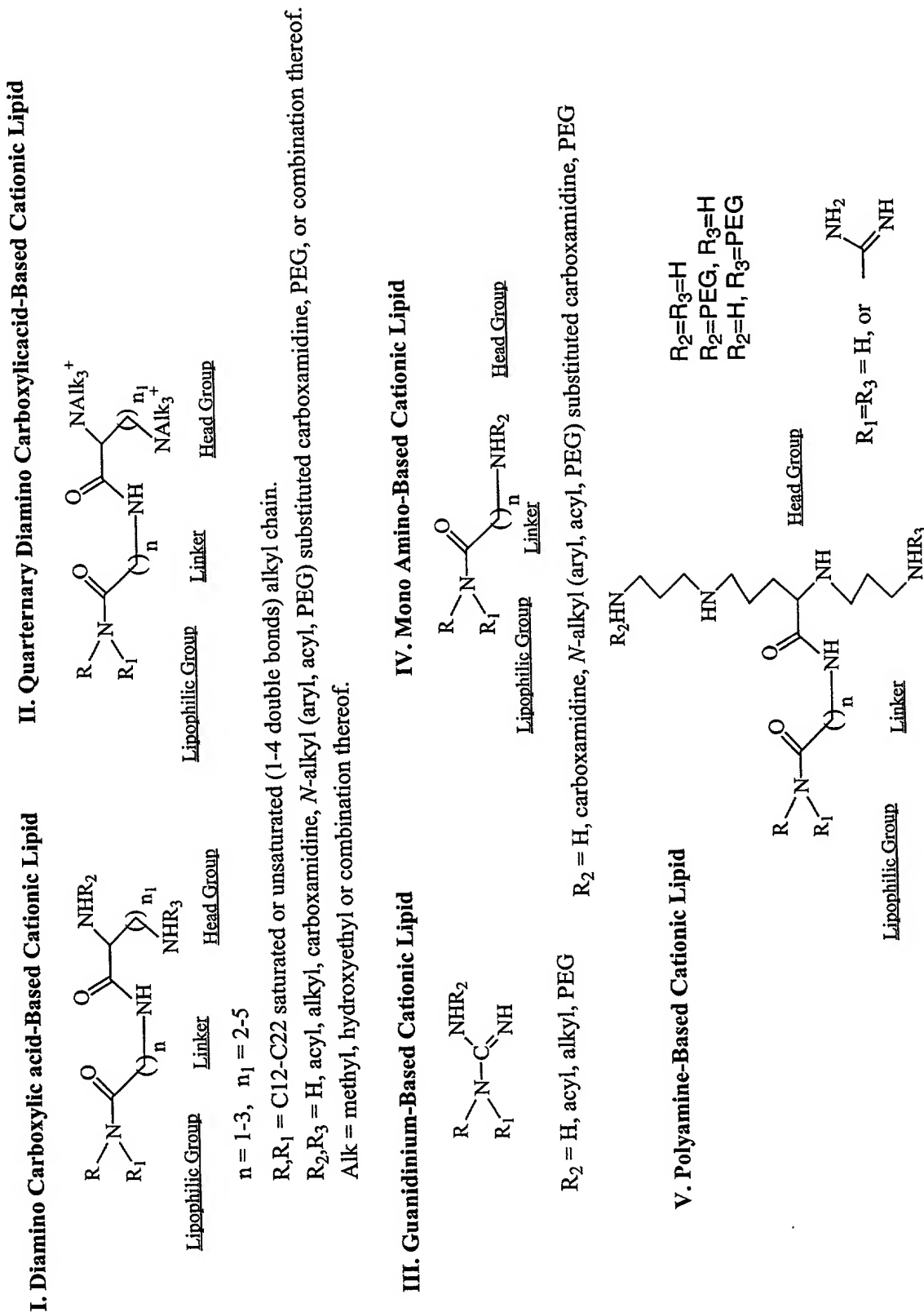
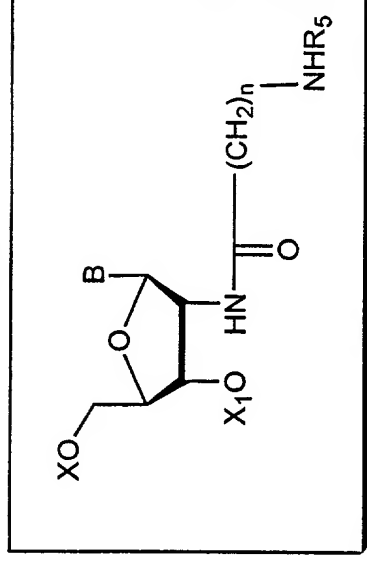
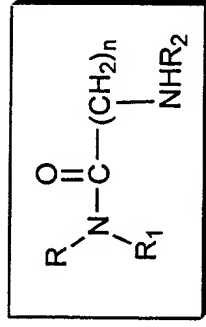


Figure 1B: Mono Amino-Based Cationic Lipid

Class V

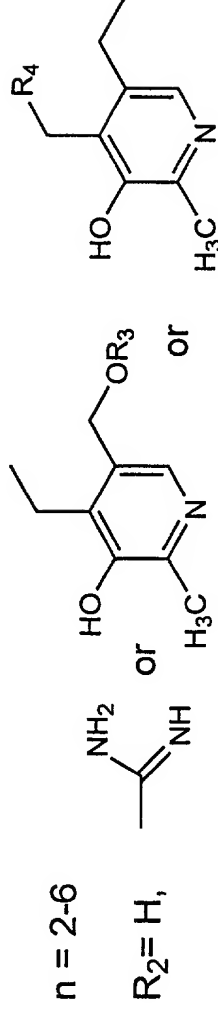


Class IV



R, R_1 = C12-C22 saturated or unsaturated (1-4 double bonds) alkyl chain.

$n = 2-6$



R_3 = H, PO_3H_2 , PEG

R_4 = OH, NH_2 , =O, O-PEG

R_5 = H, carboxamidine

$X = X_1 = R, R_1$

$X = R, X_1 = R_1, X = R_1, X_1 = R$

$X = PEG, X_1 = H$

$X = H, X_1 = PEG$

B = nucleic acid base (modified or unmodified) or H

PEG: or PEG 2000 carbonyl, PEG 5000 carbonyl

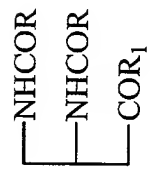
methoxypolyoxyethylene carbonyl
(Ave. Mol. Wt. = 2000 or 5000)

CO-PEG2000 - amide

COOPEG - carbamate

Figure 1C

General formula:



R = saturated or unsaturated (1-4 double bonds) alkyl chains (12-22C)

R₁ = TREN, N,N'-di-carboxamidine TREN, lysyl, arginyl, ornithyl, homoarginyl, histidyl, aminopropylimidazole, spermine carboxylic acid.

[illegible]

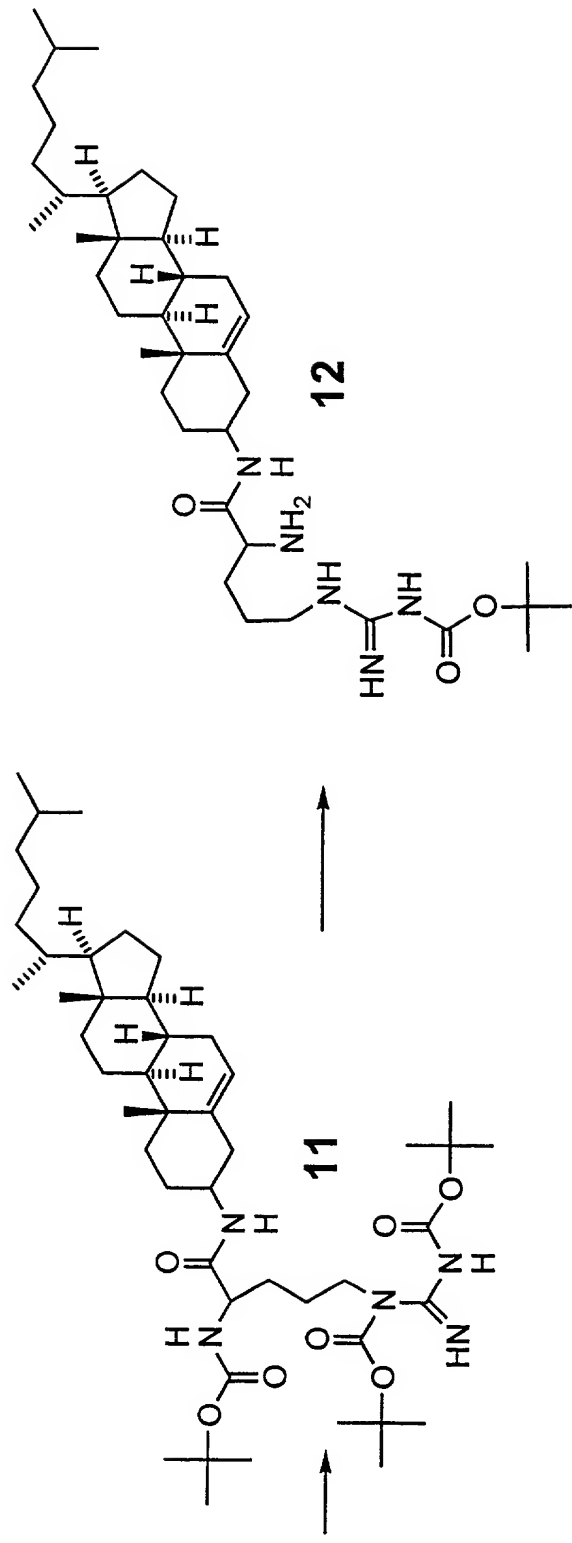




Figure 5: Synthesis of PH 55939 (17)

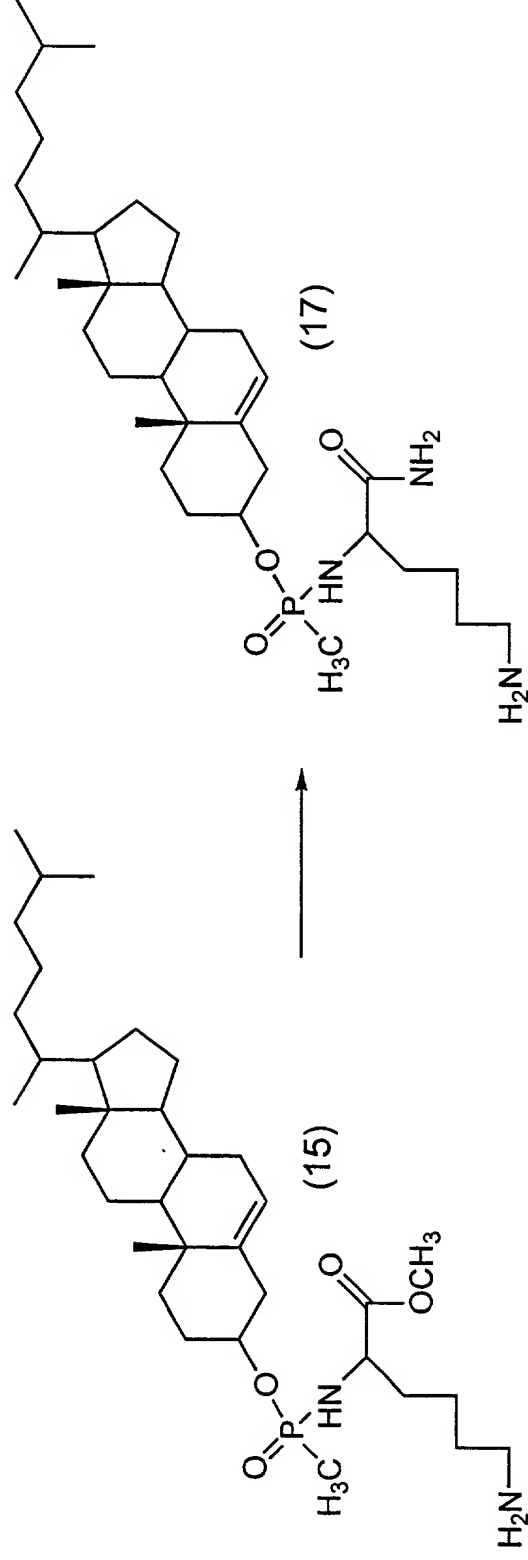


Figure 6: Synthesis of PH 55941 (18), 55942 (19)

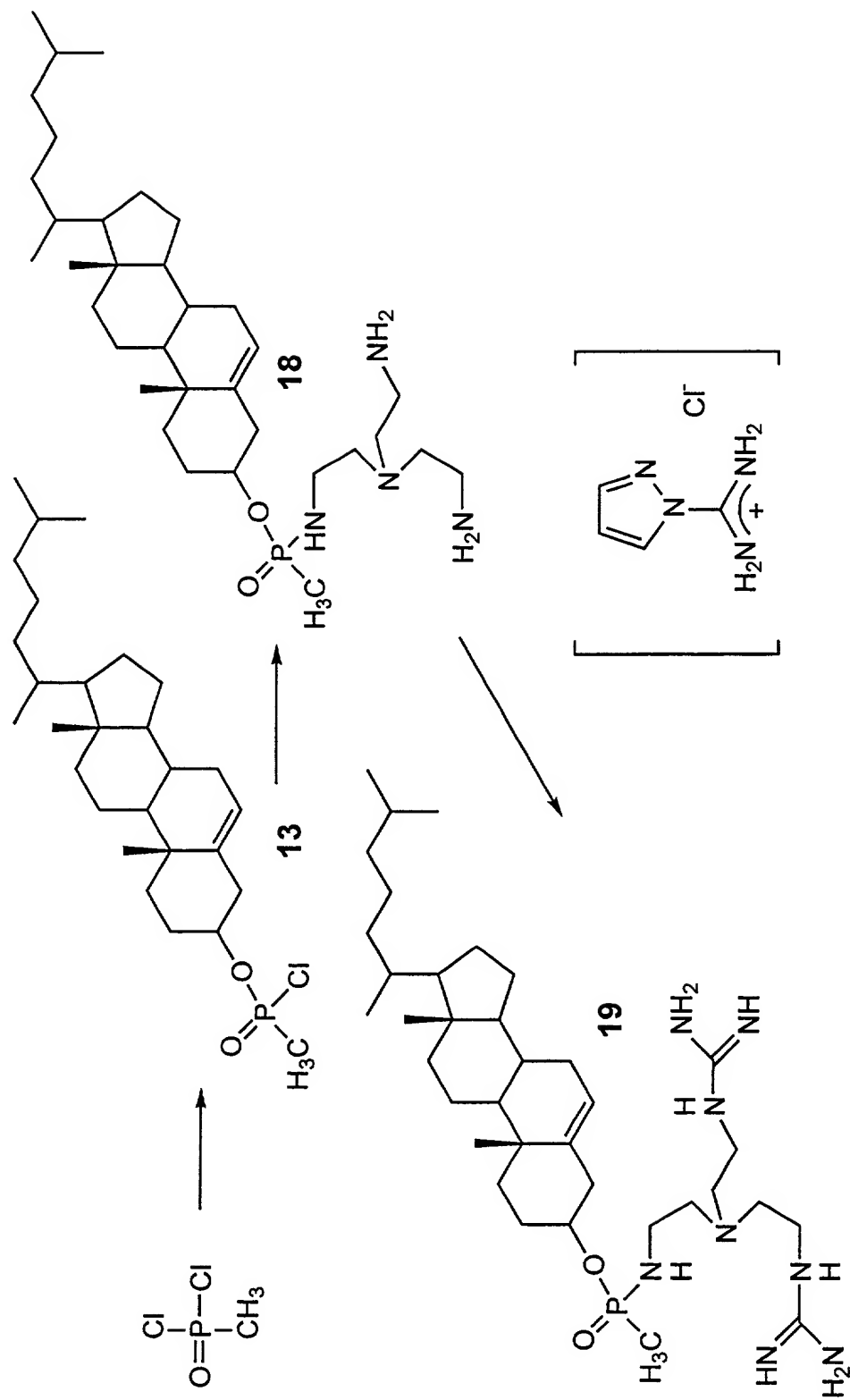


Figure 7: Synthesis of PH55943 (20)

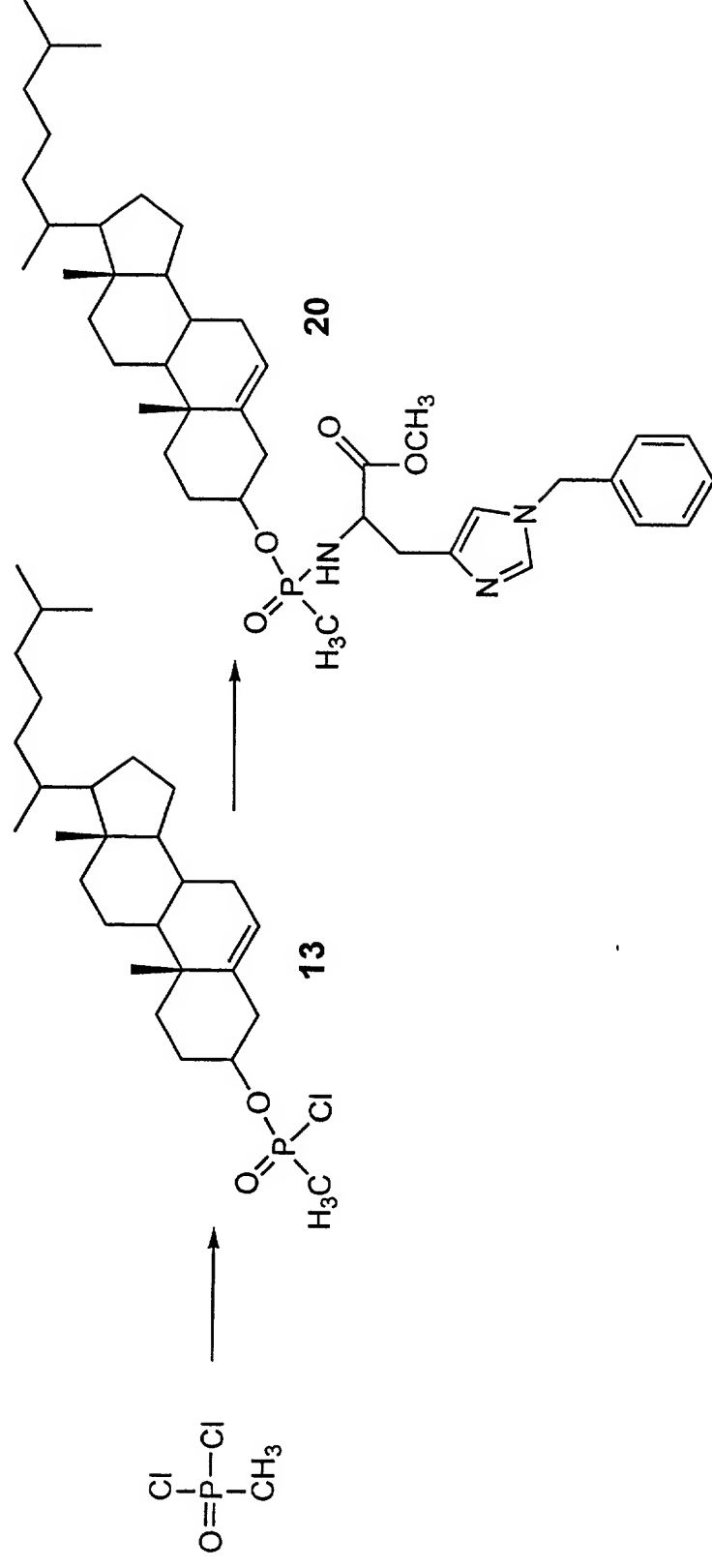


Figure 8: Synthesis of PH 55945 (21)

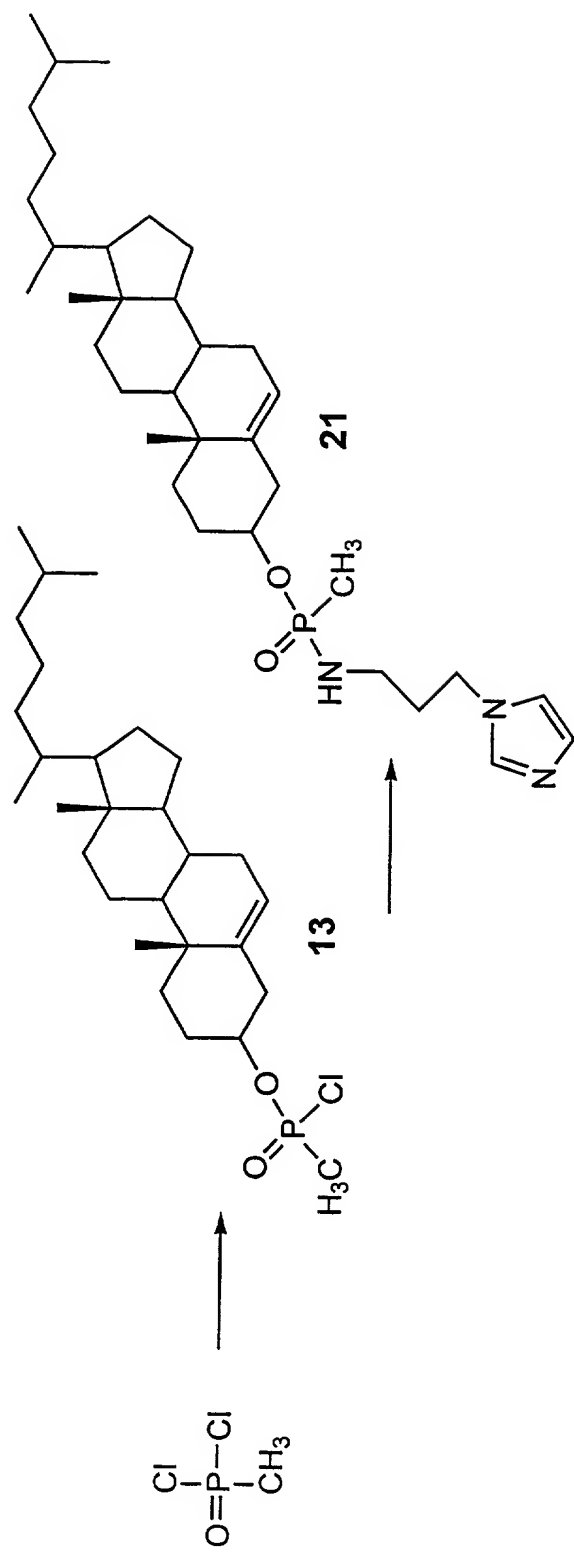
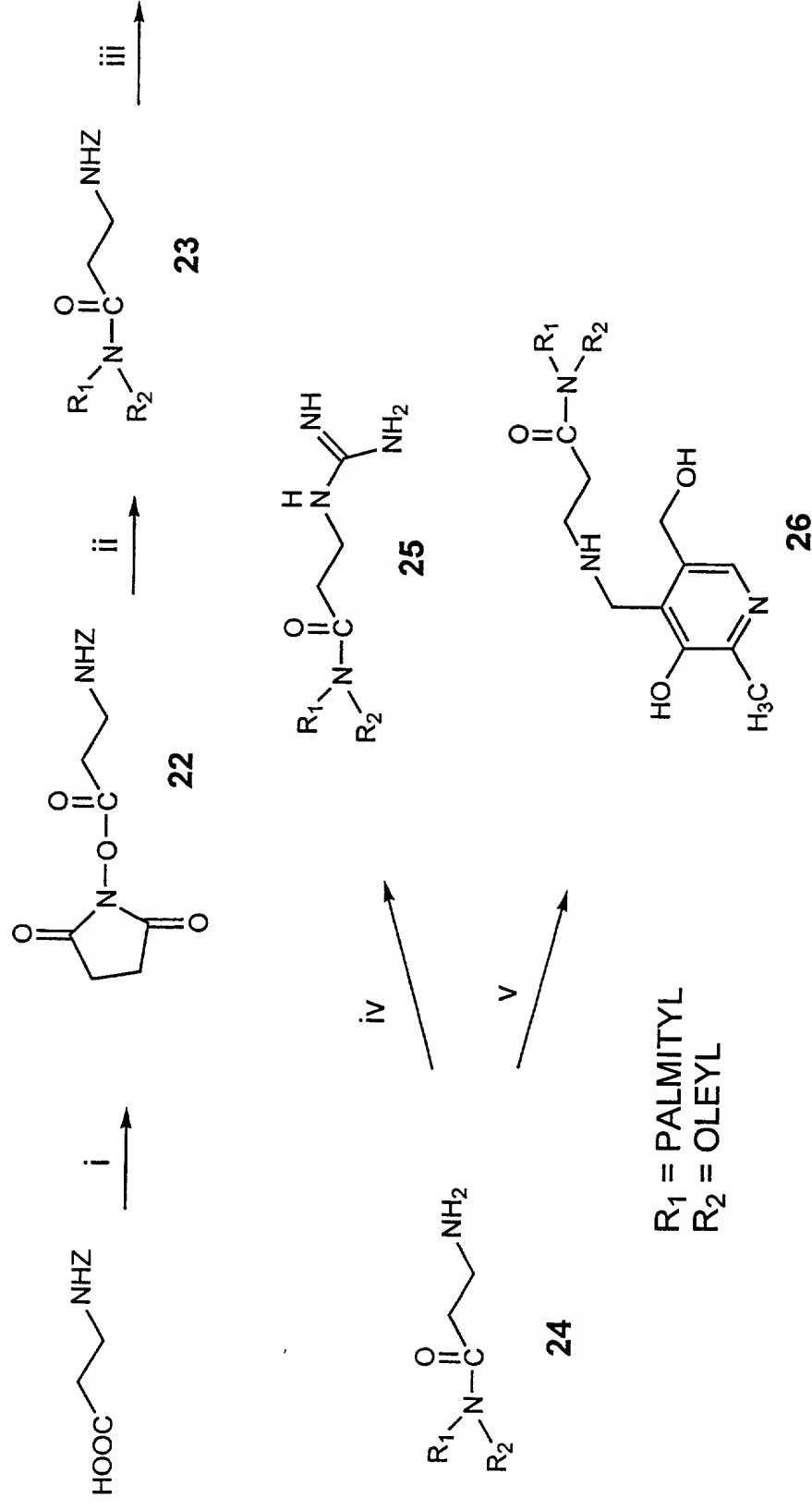
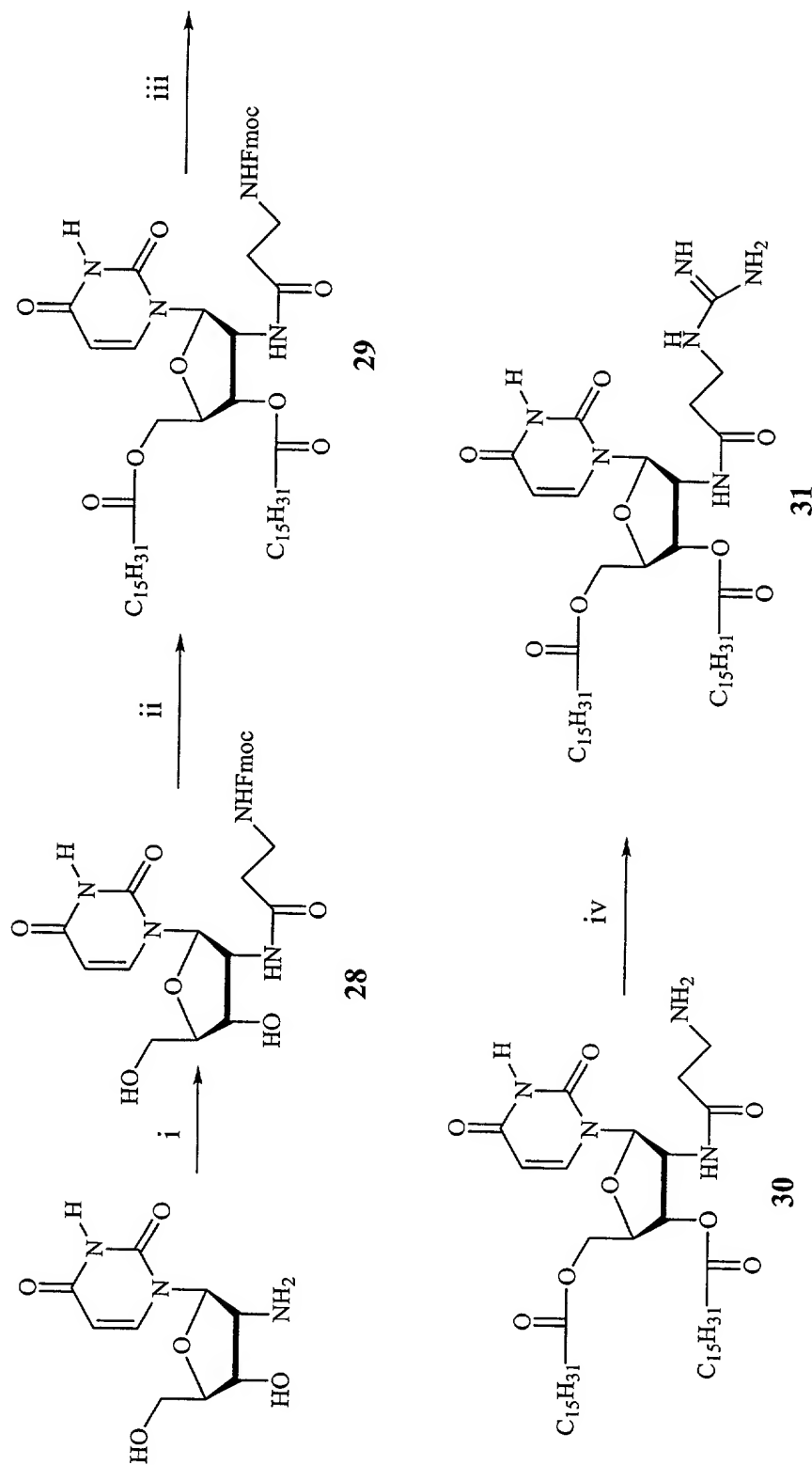


Figure 9: VITAMIN B₆ and β -Ala-BASED CATIONIC LIPIDS



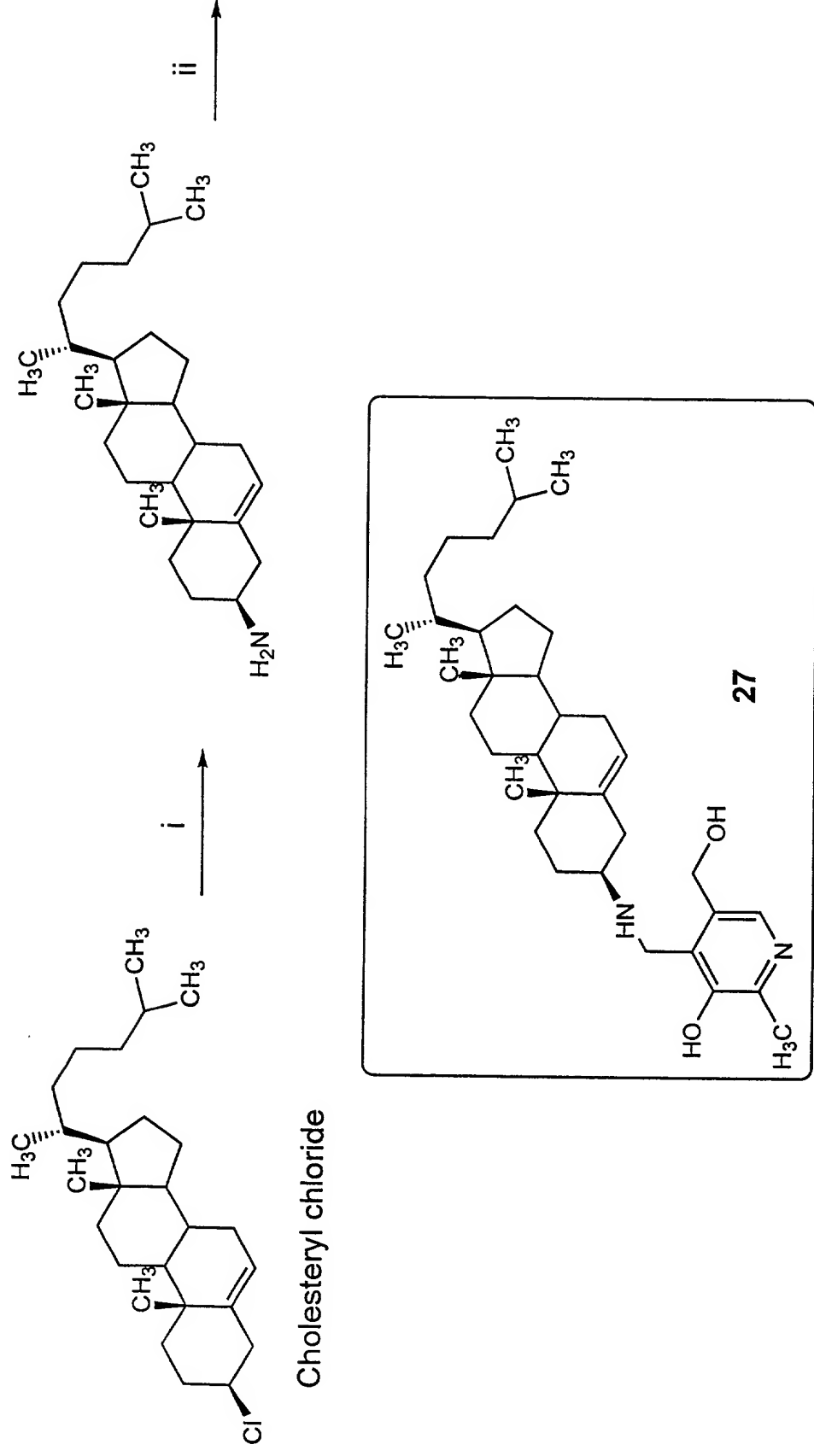
REAGENTS AND CONDITIONS: i) N-hydroxysuccinimide, DCC; ii) HNR₂, Et₃N; iii) 10% Pd/C, 1,4-cyclohexadiene; iv) a: pyridoxal/EtOH, b: NaBH₄; v) 1H-pyrazole-1-carboxamide/THF-MeOH

Figure 10



Reagents and conditions: i) N-Fmoc-b-Ala, EEDQ/MeOH; ii) $\text{C}_{15}\text{H}_{31}\text{COCl/Py}$; iii) morpholine/ CH_2Cl_2 ; iv) 1H-pyrazole-1-carboxamide/THF-MeOH

Figure 11: VITAMIN B₆-CHOLESTEROL CONJUGATE



REAGENTS AND CONDITIONS: i) NH₃/MeOH; ii) reductive amination of pyridoxal

FIGURE 12A

Group I Intron

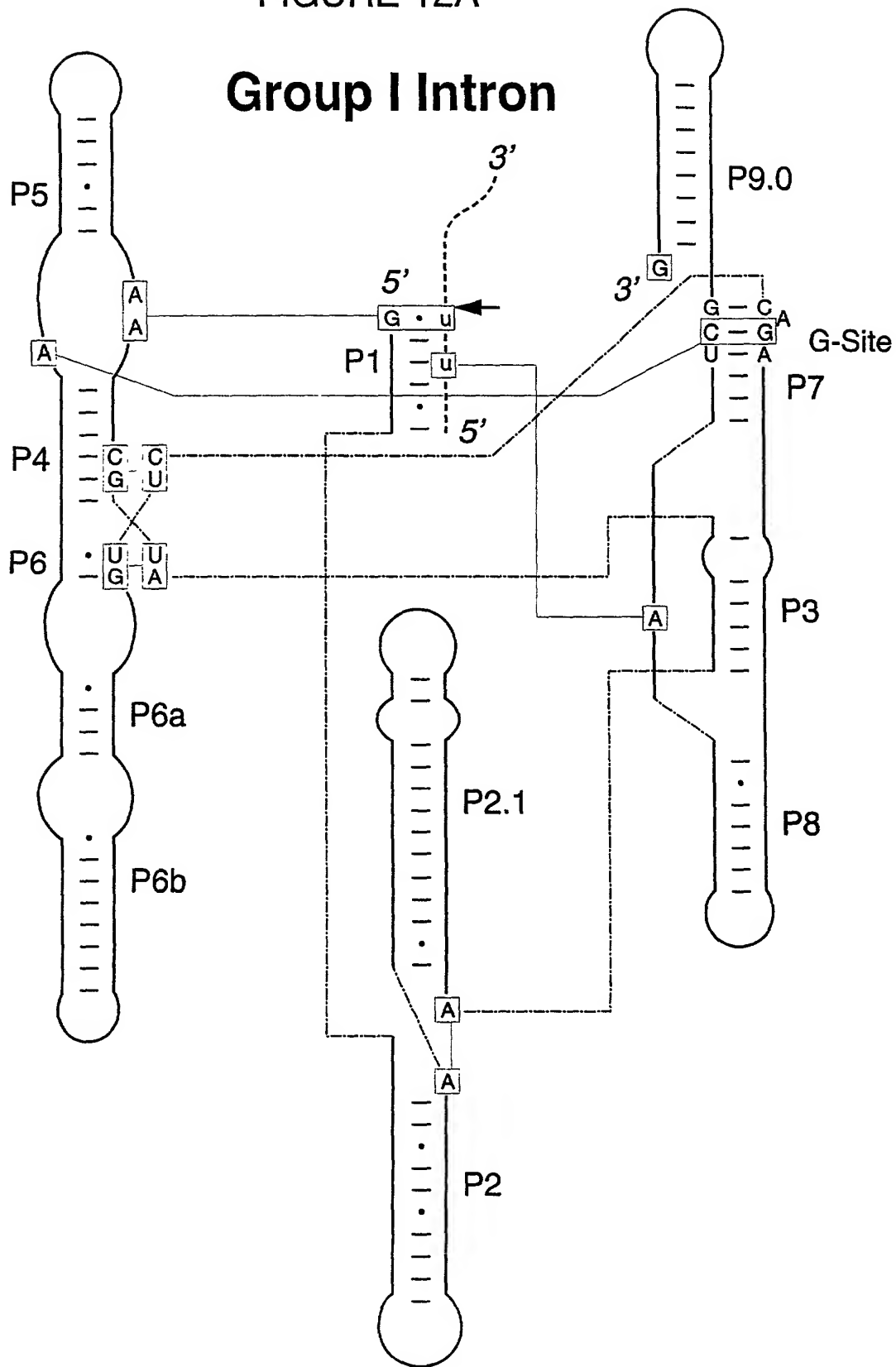


FIGURE 12B

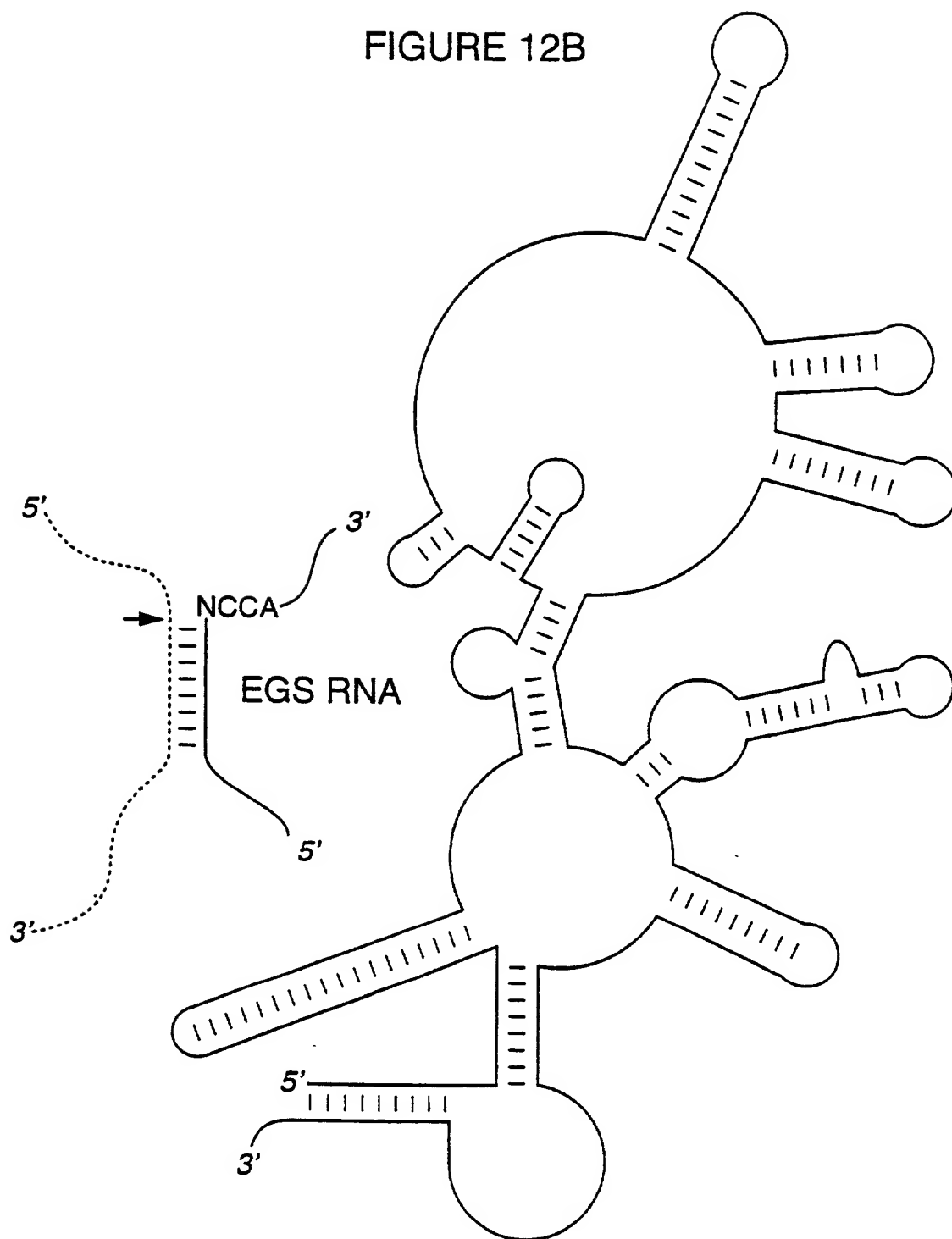


FIGURE 12C

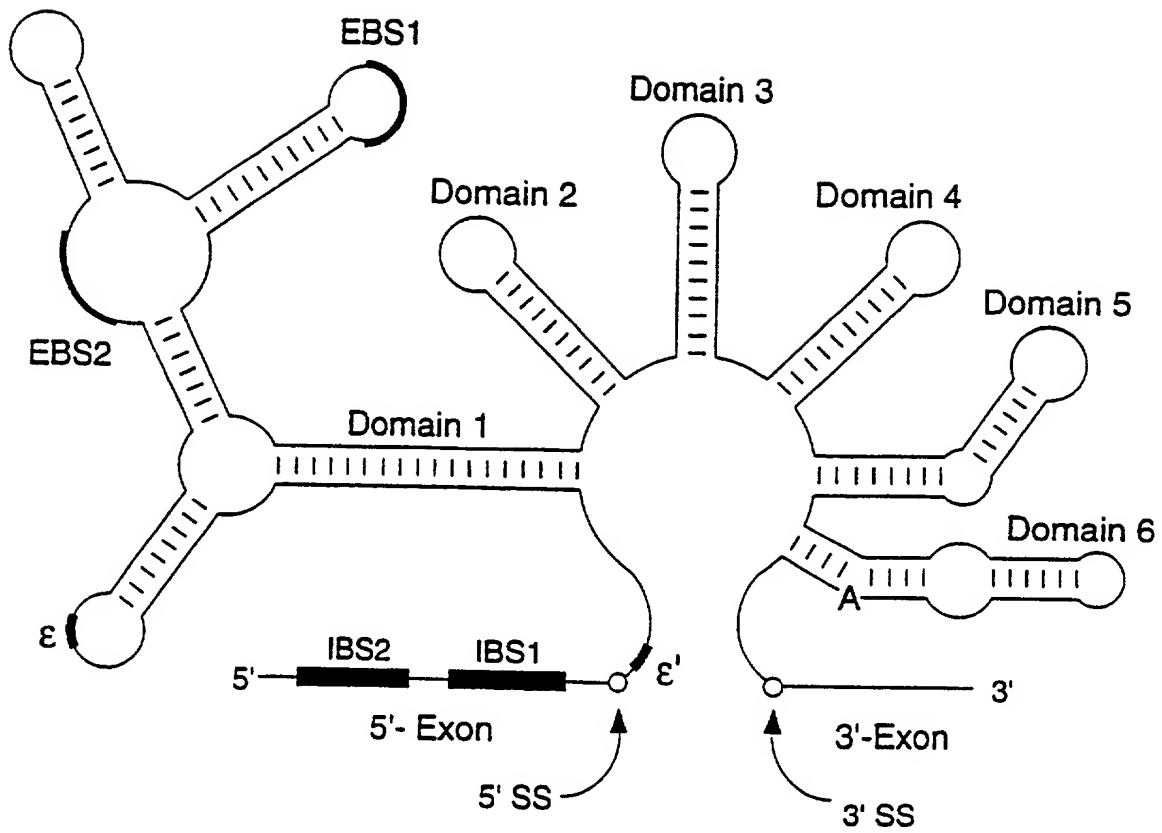


Figure 12D

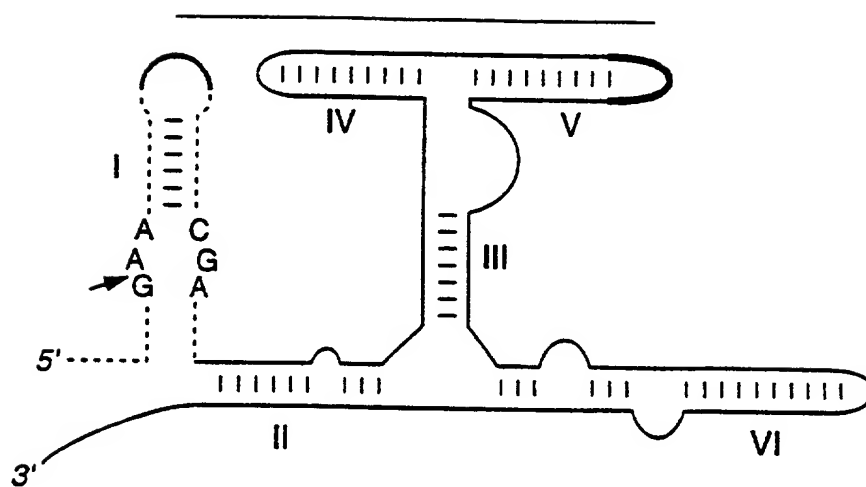


FIGURE 12E

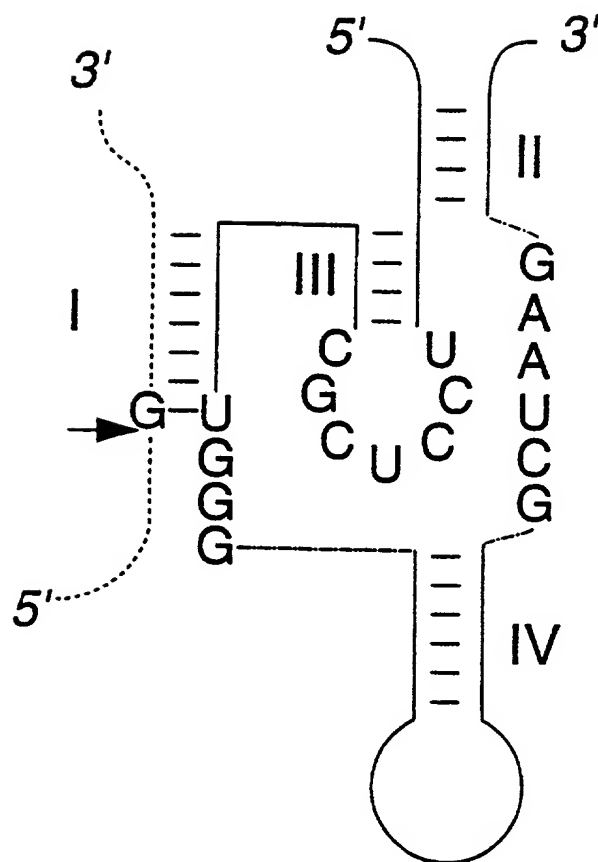


FIGURE 12F

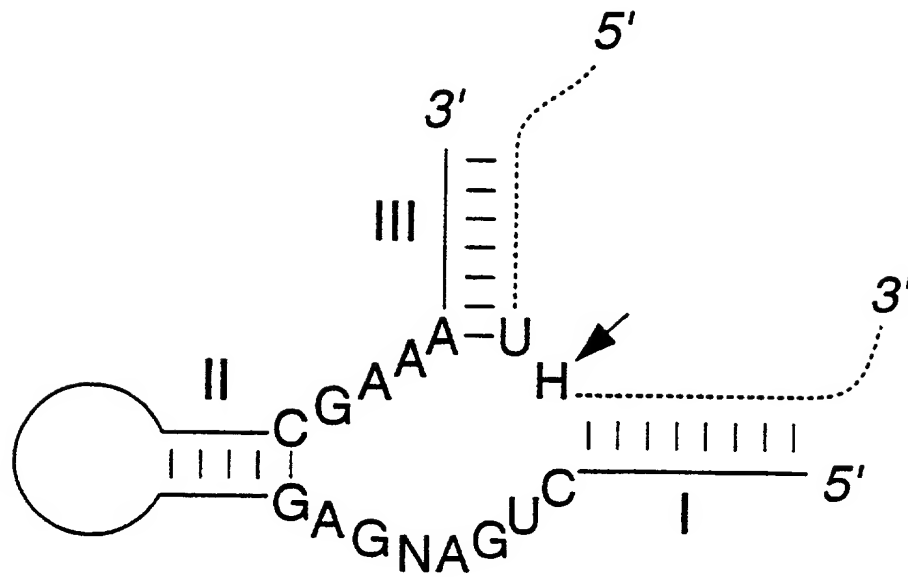
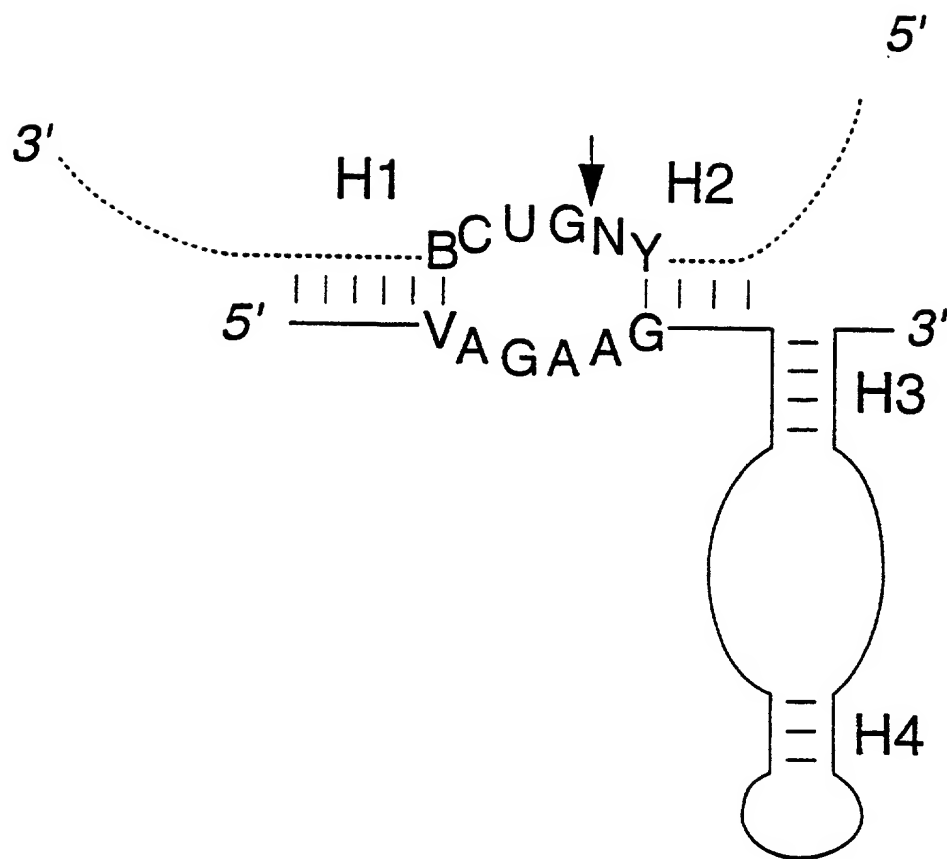


FIGURE 12G



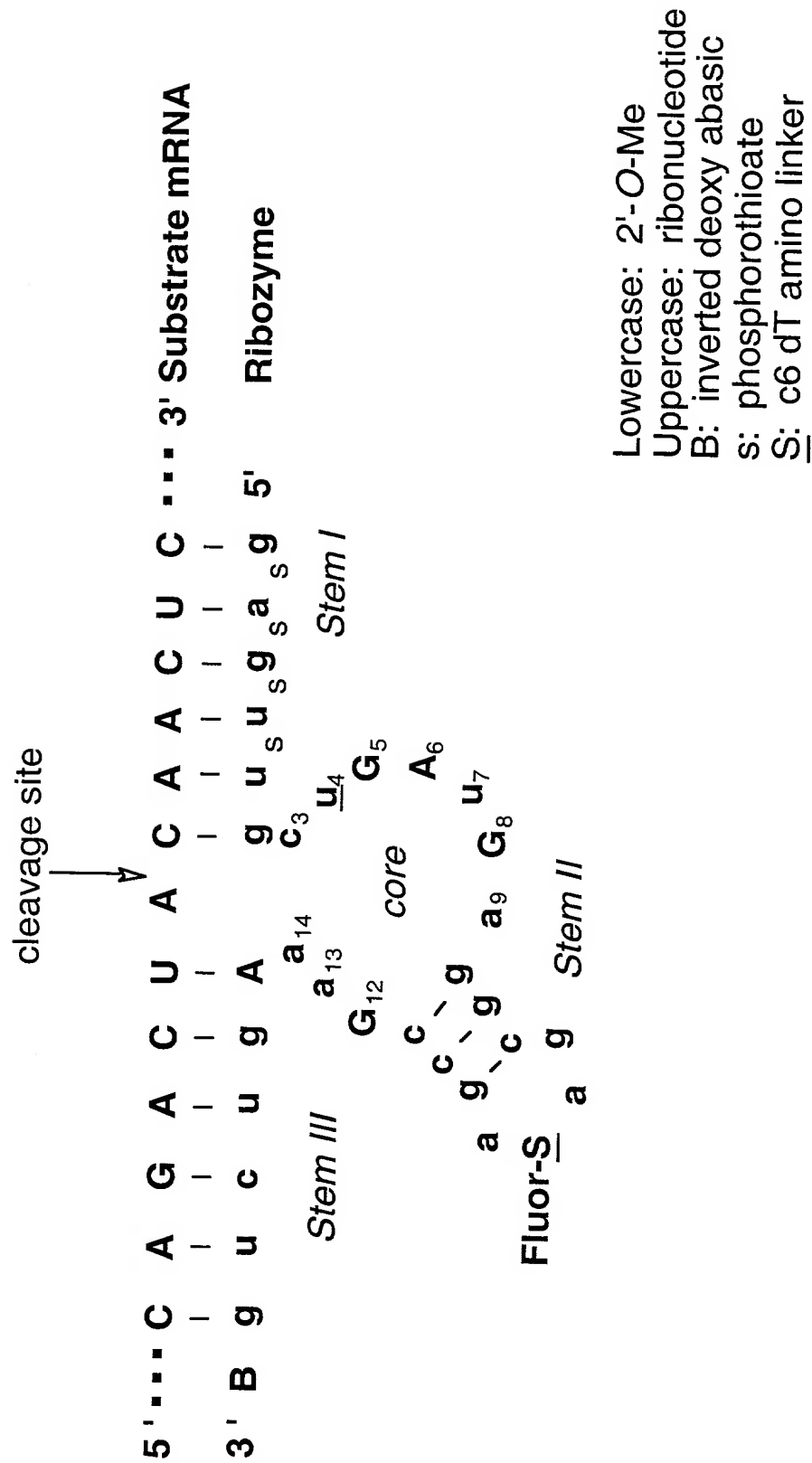
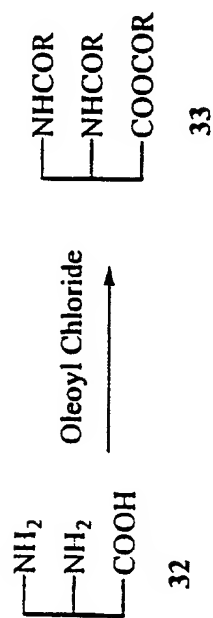


Figure 13

amide analogs



2,3-diaminopropionic acid

R = Oleyl (C_{18:1})

Figure 14

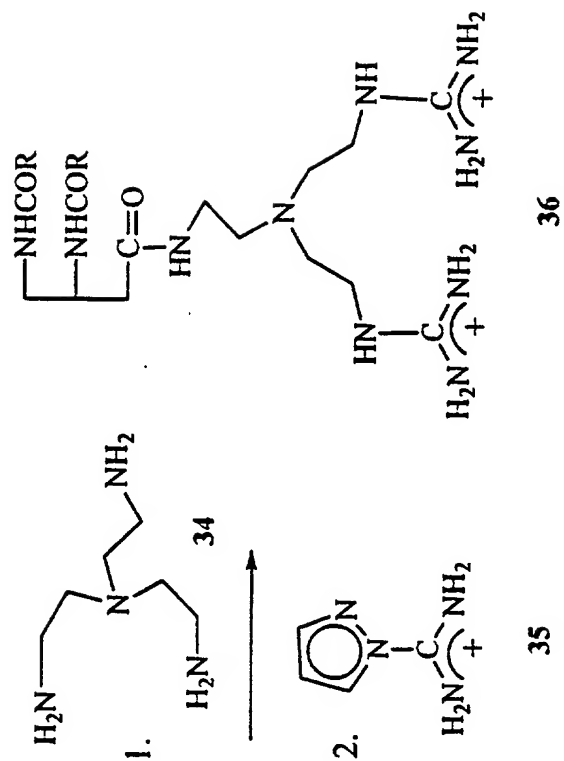
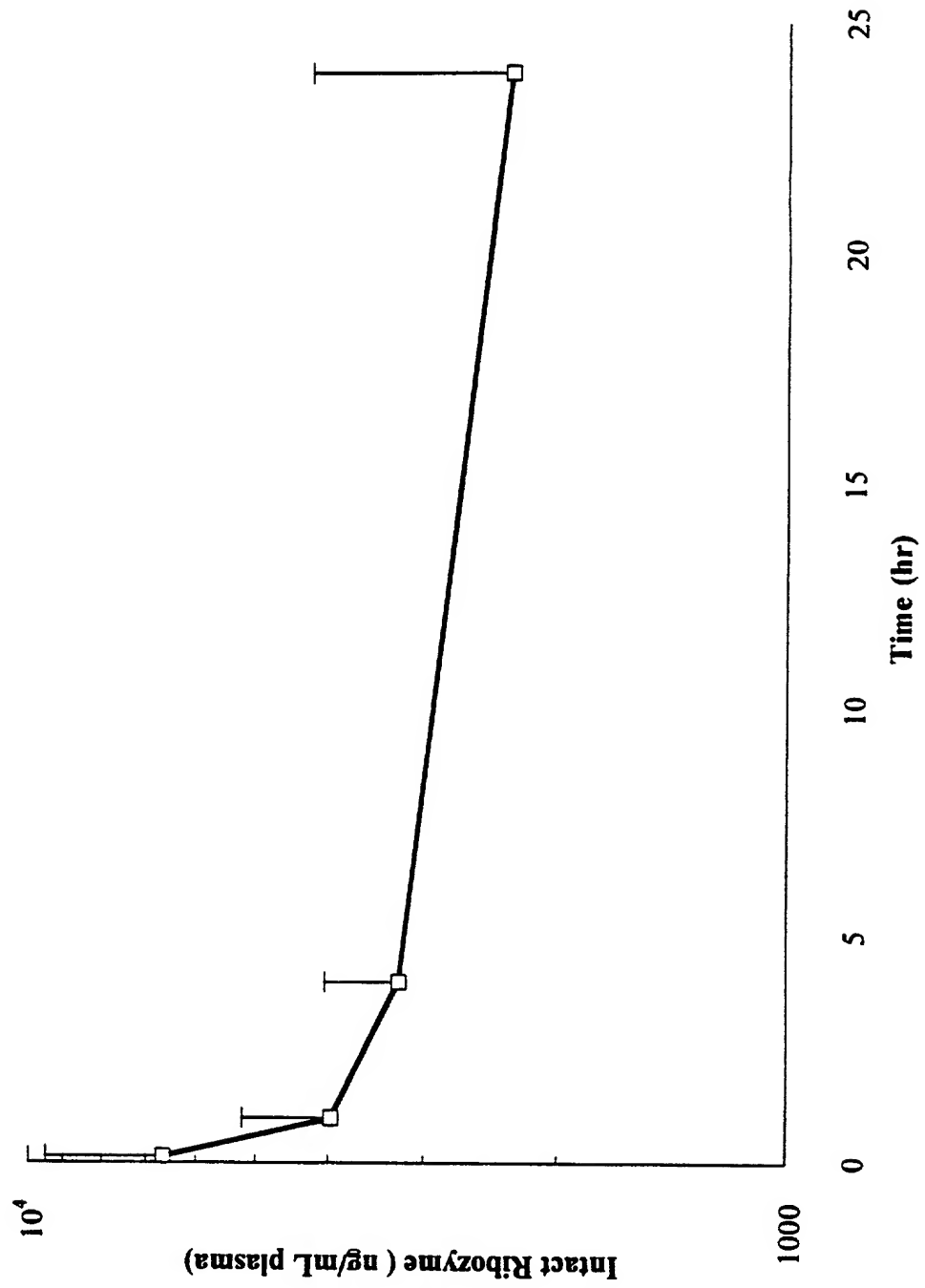


Figure 15: Concentration of Intact Ribozyme after Intravenous Administration of EPC:CHOL:DOTAP:DSPE-PEG₂₀₀₀ Liposome Encapsulated Ribozyme



**Figure 16: Inhibition of IMPDH-2 mRNA Expression in Jurkat Cells
Treated for 24 h with IMPDH antisense molecule + 5 µg/ml
Formulation ID No. 345**

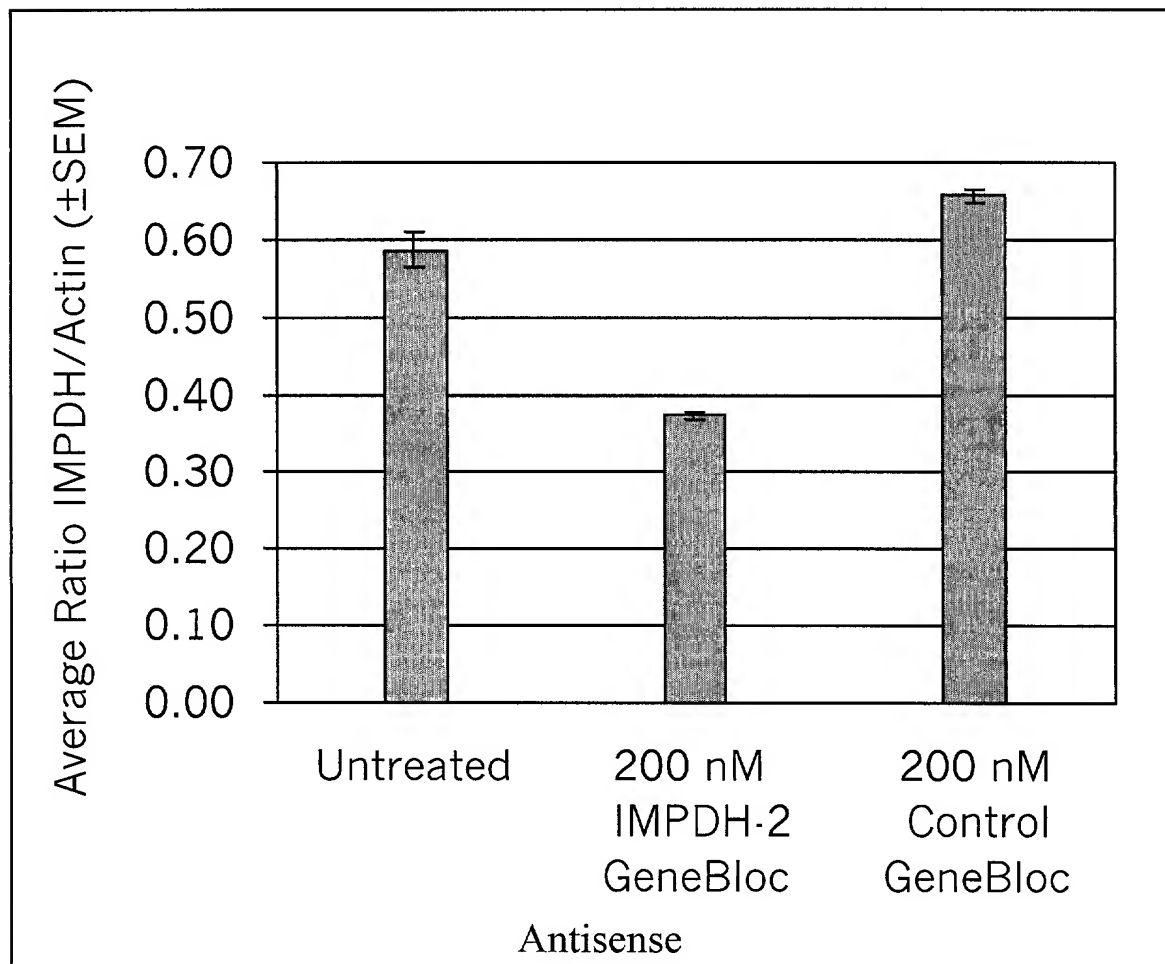


Figure 17: Inhibition of IMPDH-2 mRNA Expression in Jurkat Cells Treated for 24 h with IMPDH Antisense molecules+ Formuation ID NO: 323

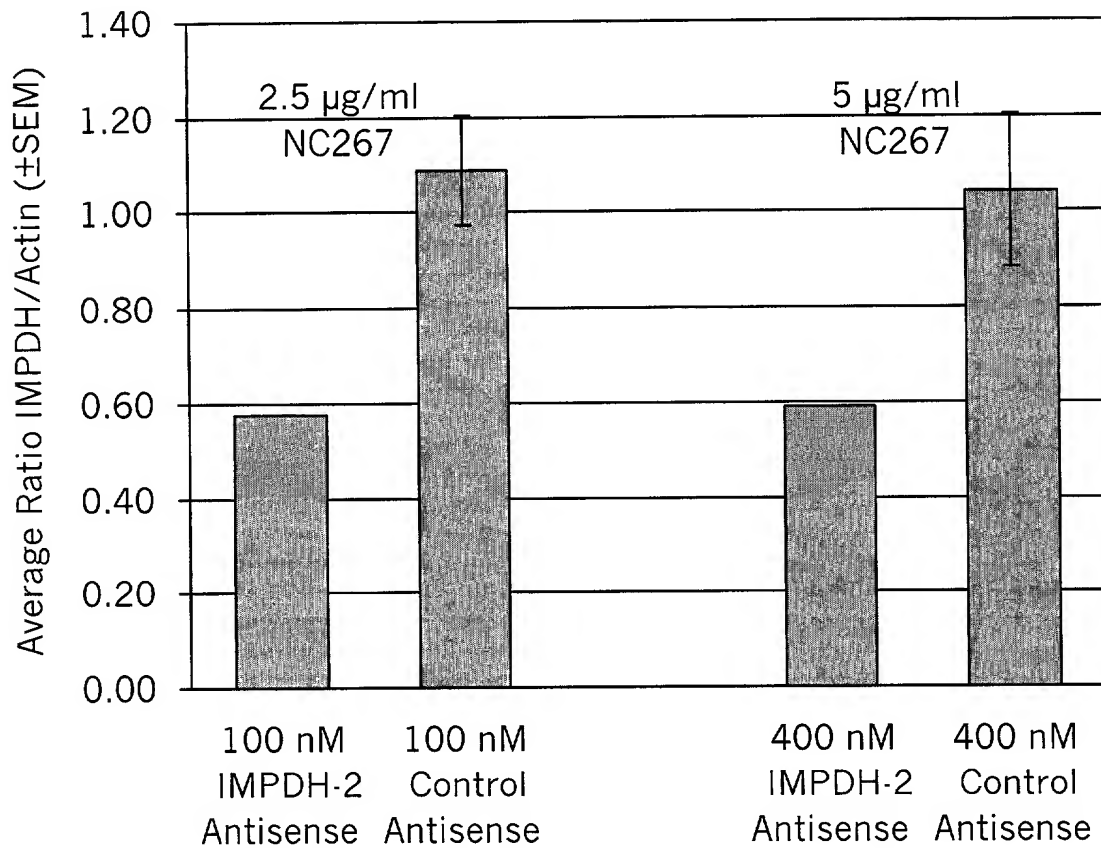


Figure 18: Inhibition of IMPDH-2 mRNA Expression in Jurkat Cells Treated for 24 h with IMPDH antisense molecules + Formulation ID NO: 333

